REMARKS

The Office Action has been carefully reviewed. No claim is allowed. Claims 5-8, 11, 23, 24, 44-48, 51, and 54-57 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 8 and 11 have been rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The examiner suggests that amendment of the claims to recite an "isolated transformed host cell" would overcome this rejection. This rejection is partly traversed with regard to claim 11 and partly obviated by the amendment to claim 8 to recite "a non-naturally occurring transformed eukaryotic or prokaryotic host cell", which indicates the presence of the hand of man.

Regarding claim 11, this claim is dependent from claim 55 which already recites an "isolated" transformed host cell. Therefore, the "transformed host cell according to claim 55" as recited in claim 11 must also be "isolated".

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 24 and 56-57 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for use of the language "sufficient length". This rejection is obviated

by the amendment to claims 24, 51, 56 and 57 to delete recitation of "sufficient length" without prejudice and instead to recite that "said antisense sequence being effective to block the expression of said polypeptide upon use", as supported in the specification at page 33, lines 10-12.

Claims 24, 51 and 56-57 have been rejected under 35 U.S.C. §112, first paragraph, as lacking written description for the recitation of "an antisense sequence of sufficient length to effectively block the expression of said polypeptide upon use". As in the above indefiniteness rejection, this new matter rejection is obviated by the amendment to claims 24, 51 and 56-57.

Claims 5-8, 11, 23-24, 44, 46-48, 51, and 54-57 have been rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description. The examiner states that one would reasonably conclude that the specification does not disclose which fragment of SEQ ID NO:1 is responsible for potentiating cell death or which analog of SEQ ID NO:1 potentiates cell death. The examiner further takes the position that the specification does not provide adequate written description of an antisense sequence of sufficient length to effectively block the expression of SEQ ID NO:1. This rejection is respectfully traversed.

Regarding the antisense sequence, the claims are amended to delete the recitation of "sufficient length". The examiner's attention is respectfully directed to Example 15 on antisense in the USPTO Synopsis of Application of Written Description Guidelines, where it is taught in the analysis provided that the sample specification indicates that the complement of SEQ ID NO:1 is essential to the operation of the claimed invention, as is the case in the present application. The analysis states that:

> The general knowledge in the art is that any full-length complement of a target mRNA inhibits the function of the mRNA and is therefore an antisense oligonucleotide. Thus, one of skill in the art would view applicant's disclosure of a coding sequence, with the statement that the invention includes antisense oligonucleotides as an implicit disclosure that the full-length complement of SEQ ID NO:1 is an antisense oligonucleotide.

The analysis concludes by stating that, considering the specification's disclosure of:

(1) the sequence (SEQ ID NO:1) which defines and limits the structure of any effective antisense molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim, and

(2) the functional characteristics of the claimed invention as well as a routine art-recognized method for screening for antisense molecules which provide further

distinguishing characteristics of the claimed invention, along with

(3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention. Accordingly, the presently claimed antisense sequence is adequately described.

Regarding adequate written description of a fragment of SEQ ID NO:1 or an analog of the polypeptide of SEQ ID NO:1, the present specification discloses on page 23, lines 15-16 that "acceptable analogs are those which retain at least the prodomain (CARD)". Accordingly, the no more than ten single residue changes to the amino acid sequence of SEQ ID NO:1, as recited in claim 44 subpart(b), would be outside the CARD domain. Ten single residue changes means that, for a full length 540 residue polypeptide encoded by SEQ ID NO:1, the claimed analog would have greater than 98% sequence identity. As taught by Example 14 (Product by Function) of the USPTO Synopsis of Application of Written Description Guidelines, one of skill in the art would conclude from the single species (i.e., SEQ ID NO:1) that the single species disclosed is representative of the entire genus because all member have at least 95% (here, it is at least 98%) structural identity to the reference sequence of SEQ ID NO:1 and have a specific activity (i.e., potentiating cell death) that is readily

assayable (see the cell death assay disclosed in the paragraph bridging pages 58 and 59 of the present specification).

Regarding fragments of SEQ ID NO:1, Fig. 5 clearly demonstrates that it is the CARD domain, and not the other regions of the B1 protein of SEQ ID NO:1, that is necessary and sufficient to potentiate cell death. The present specification discloses at page 59, lines 25-29, that "at least the CARD domain is involved in the potentiation of cell death, possibly together with the intermediate domain". Thus, the issue of whether or not potentiation occurs by binding of CARD to BCL2 is not critical to the question of whether this domain in the B1 protein of SEQ ID NO:1 potentiates cell death. The fragments ΔNde and ΔK shown in Fig. 5 are representative of the genus of fragments of SEQ ID NO:1 that potentiates cell death.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 5-8, 11, 23-24, 44, 46-48, 51, and 54-57 remain rejected under 35 U.S.C. §112, first paragraph, because the examiner states that, while enabling for the polynucleotide of SEQ ID NO:2 or polynucleotide encoding SEQ ID NO:1, the present specification lacks enablement for a DNA sequence consisting essentially of sequence encoding a polypeptide analog or fragment of SEQ ID NO:1, which analog or

fragment potentiates cell death. This rejection is respectfully traversed.

As indicated in the previous response, this issue is ripe for appeal. Applicants incorporate by reference the arguments made in the amendment of October 7, 2003, at pages 15-23 and in the amendment of May 2, 2005, at pages 17-18.

Furthermore, based on the disclosure in Fig. 5 and in the specification as discussed above insofar as written description is concerned, one of skill in the art is taught that acceptable analogs are those which retain at least the CARD domain. Accordingly, given this guidance in the specification, one of skill in the art would naturally target regions outside of the CARD domain for change in order to generate variants or for deletion to generate fragments. In addition, the specification at page 53, lines 12-15, teaches that the prodomain CARD structure is common to a number of prior art intracellular proteins involved in apoptotic signaling pathways, citing as examples c-IAP1, RAIDD, ICE, and ICH-1. Examination and comparison of such a CARD domain and other regions in these other intracellular proteins would offer further clues that would guide one of skill in the art to even make conservative substitutions in the CARD region.

Therefore, the presently claimed invention is fully enabled by the present specification, given the high level of skill in the art.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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